Prediction of 14-year cardiovascular outcomes by dobutamine stress ^{99m}Tc-tetrofosmin myocardial perfusion SPECT in elderly patients unable to perform exercise testing

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Background. **Dobutamine stress myocardial perfusion imaging (MPI) is a useful alternative for the evaluation of coronary artery disease (CAD) in elderly patients who are unable to perform an exercise stress test. However, data on the long-term prognostic value of stress MPI in elderly patients are lacking. Therefore, this study evaluated the long-term prognostic value of dobutamine stress MPI in elderly patients unable to perform an exercise test.**

Methods. **The study population consisted of 247 elderly patients (mean age 71 ± 5 years) who underwent dobutamine stress single-photon emission computed tomography (SPECT) MPI. An abnormal SPECT study was defined as the presence of fixed and/or reversible perfusion defects. A summed stress score (SSS) was obtained to estimate the extent and severity of perfusion defects. End points during follow-up were all-cause mortality, cardiac mortality, and nonfatal myocardial infarction (MI).**

Results. **During a median follow-up of 14 years (range 12-16), 168 (68%) patients died (all-cause mortality), of which 56 (23%) were due to cardiac causes. Nonfatal MI occurred in 19 (8%) patients. Kaplan-Meier survival curves showed that MPI provided optimal risk stratification in patients with normal and abnormal MPI. Multivariable analysis identified an abnormal MPI as a strong significant predictor of all-cause mortality and cardiac events. A multivariable analysis also revealed that a reversible defect and SSS were strong long-term predictors of cardiac mortality and hard cardiac events.**

Conclusion. **Dobutamine stress ^{99m}Tc-tetrofosmin SPECT provides incremental prognostic information for the prediction of long-term cardiovascular outcomes in elderly patients, unable to perform exercise testing. Dobutamine stress MPI is useful in risk classifying elderly patients. (J Nucl Cardiol 2018;25:63–71.)**

Key Words: ^{99m}Tc-tetrofosmin • dobutamine stress SPECT • long-term prognosis • coronary artery disease • elderly

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Abbreviations	
ACE	Angiotensin converting enzyme
CABG	Coronary artery bypass graft surgery
CAD	Coronary artery disease
ECG	Electrocardiography
MI	Myocardial infarction
MPI	Myocardial perfusion imaging
LBBB	Left bundle branch block
PCI	Percutaneous coronary intervention
SPECT	Single-photon emission computed tomography
SSS	Summed stress score

See related editorial, pp. 72–74

INTRODUCTION

Globally, deaths from cardiovascular disease are increasing, in particular, due to the aging population. Between 1990 and 2013, the number of global deaths caused by cardiovascular disease has increased by 41%.[1] As a result of aging of the population, more elderly patients are referred for diagnostic and prognostic cardiac evaluation. Stress myocardial perfusion imaging (MPI) is useful for the evaluation of coronary artery disease (CAD) in elderly patients.[2,3] A substantial proportion of the elderly population is unable to perform exercise stress testing, because of conditions such as degenerative joint disease or peripheral vascular disease. In such patients, vasodilator stress testing is a useful alternative. In patients who also have contraindications for vasodilator stress (such as reactive airway disease or high-grade atrioventricular nodal block), dobutamine stress MPI is recommended according to the ASNC imaging guidelines for nuclear cardiology.[4] The prognostic value of MPI using single-photon emission computed tomography (SPECT) with ^{99m}Tc-tetrofosmin or ^{99m}Tc-sestamibi as tracers in elderly patients has been studied previously for short- and medium-term follow-up.[5-9] Long-term prognostic data to define the role of stress MPI for the prediction of cardiovascular outcomes in elderly patients are lacking. The long-term prognostic value of stress MPI in elderly patients may be impaired because of their increased underlying cardiovascular risk. Accordingly, the aim of the current study was to assess the long-term prognostic value of dobutamine stress ^{99m}Tc-tetrofosmin MPI for the prediction of cardiovascular outcomes in elderly patients unable to perform exercise testing.

METHODS

Study Population

This study included 272 consecutive elderly patients ≥65 years old who were unable to perform exercise testing and underwent dobutamine stress 99mTc-tetrofosmin SPECT for the evaluation of suspected or known CAD. The age cut-off was based on previous studies.[3,10] The current study is a continuation of a previous study [8] in which this population of elderly patients was evaluated with a mean follow-up of 3 years The reason to perform the current follow-up study was to assess the very long-term prognostic value of dobutamine stress SPECT. At the time of this study, dobutamine was the preferred stressor in our nuclear cardiology laboratory, and the mode of stress was determined by the referring physician. Patients were enrolled between 1995 and 1999. Follow-up was complete for 270 (99.3%) patients. Twenty-three patients underwent coronary artery revascularization <60 days of the test and were excluded. This exclusion was based on previous data indicating that in the first 60 days after the test, referral for coronary artery revascularization tends to be based on the SPECT results, whereas >60 days after testing, referral for coronary artery revascularization tends to be based on deterioration of the patient's clinical status.[11] The present data are based on 247 patients. This study was not subject to the Dutch Medical Research Involving Human Subjects Act.[12,13] Therefore, approval from the local research ethics committee to conduct this retrospective study was not required at the time of enrollment. Moreover, the study was conducted according to the Declaration of Helsinki.[14] All patients consented participation in this study.

Clinical Data

Before dobutamine stress testing, a structured clinical interview and history were acquired, and cardiac risk factors were assessed. Hypertension was defined as a blood pressure ≥140/90 mmHg or treatment with antihypertensive medication. Diabetes mellitus was defined as a fasting glucose level ≥7.8 mmol·L^{-1} or the need for insulin or oral hypoglycemic medication. Hypercholesterolemia was defined as a total cholesterol ≥6.4 mmol·L^{-1} or treatment with lipid-lowering medication.

Dobutamine Stress Testing

Dobutamine stress testing was performed according to a standard protocol as previously reported.[15] Dobutamine was infused through the antecubital vein, starting with a dose of 10 μg·kg^{-1}·min^{-1} for 3 minutes and being increased by 10 μg·kg^{-1}·min^{-1} every 3 minutes up to a maximum dose of 40 μg·kg^{-1}·min^{-1}. If the test endpoint was not reached at a dobutamine dose of 40 μg·kg^{-1}·min^{-1}, atropine (up to 1 mg) was given intravenously. Blood pressure and heart rate were monitored, and electrocardiography was recorded constantly. Test endpoints were achievement of target heart rate (85% of maximum age- and sex-predicted heart rate); horizontal or

downsloping ST-segment depression >2 mm at an interval of 80 ms after the J-point, compared with baseline; ST-segment elevation >1 mm in patients without previous myocardial infarction; severe angina; a systolic blood pressure fall >40 mm Hg, compared with baseline; blood pressure >240/120 mmHg; or significant cardiac arrhythmias. Metoprolol was available to reverse the adverse effects of dobutamine/atropine.

^{99m}Tc-Tetrofosmin SPECT MPI

Approximately 1 min before the termination of the dobutamine stress test, an intravenous dose of 370 MBq of ^{99m}Tc-tetrofosmin was administered. For resting studies, 370 MBq of tetrofosmin were injected at least 24 hours after the stress study. Image acquisition was performed with a triple-head γ-camera system (Prism 3000 XP; Picker International). For each study, six oblique (short axis) slices from the apex to the base and three sagittal (vertical long axis) slices were defined. Each of the six short-axis slices was divided into eight equal segments. Owing to correspondence of the septal part of the two basal slices to the fibrous portion of the interventricular septum and normally exhibits reduced uptake, this region was excluded from analysis. As a consequence, 47 segments were identified (3 long axis and 44 short axis). The interpretation of the scan was semiquantitatively performed by visual analysis and aided by circumferential profiles analysis. Stress and rest tomographic views were reviewed side by side by an experienced observer who had no knowledge of the patients' clinical information. A reversible perfusion defect was defined as a perfusion defect on the exercise images that partially or completely resolved at rest in ≥2 contiguous segments or slices. A fixed perfusion defect was defined as a perfusion defect on exercise images in two or more contiguous segments or slices, which persists on rest images. The presence of a fixed and/or reversible perfusion defect was considered as an abnormal study. Each myocardial segment was assigned a score from 0 to 3 (0 = normal; 1 = slightly reduced; 2 = moderately reduced; 3 = severely reduced or absent uptake). Summed stress score (SSS) was calculated by the summation of the scores of the myocardial segments at stress. Standard 17-segment-based scores were calculated and converted to percent of the total myocardium (% myocardium) by dividing the summed scores by the maximum potential score, and multiplying by 100.[16]

Patient Follow-up

Collection of follow-up data was performed by contacting the patient, the patient's general practitioner, civil registries, and review of hospital records. Follow-up data were obtained in September 2011. The date of the last review or consultation was used to determine follow-up time. Endpoints were all-cause mortality, cardiac mortality, and nonfatal myocardial infarction (MI). Causes of death were obtained from the Central Bureau of Statistics Netherlands. Cardiac mortality was defined as death caused by myocardial infarction, significant cardiac arrhythmias, or refractory congestive heart failure. Sudden death occurring without another explanation was included as cardiac mortality. Nonfatal MI was described by chest pain complaints, the rise and fall of cardiac marker levels and typical changes on electrocardiography (ECG). Hard cardiac events were defined as the occurrence of cardiac mortality or nonfatal MI.

Statistical Analysis

Continuous data were expressed as mean ± SD, and percentages were rounded. Continuous variables were compared using the Student t test for unpaired samples. The cumulative survival was calculated using the Kaplan-Meier method. Survival curves were compared with the log-rank test. Univariable and multivariable Cox proportional hazards regression models were used to investigate the additional value of MPI parameters. The risk of a variable was expressed as a hazard ratio (HR) with a corresponding 95% confidence interval. First, clinical data were selected in a stepwise forward selection manner with entry and retention set of a significance level of 0.05. Significant clinical data were then used for including in the multivariable analysis. The incremental value of MPI over the clinical variables in the prediction of events was determined according to 3 models. In Model 1, the incremental values of abnormal MPI over the clinical data and stress test information were assessed. In Model 2, the presence of a fixed or reversible defect was entered. In Model 3, the SSS was entered. A P value $< .05$ was considered statistically significant.

RESULTS

Demographics and Stress Test Results

Clinical characteristics of the 247 patients are presented in Table 1. The mean age of the study population was 71 ± 5 years (range 65 and 86 years). A total of 48 patients (19%) were >75 years old. Dobutamine stress increased heart rate significantly (from 72 ± 15 to 128 ± 16 bpm, $P < .001$) and increased systolic blood pressure modestly (from 140 ± 23 to 146 ± 31 mm Hg, $P < .001$). The highest dobutamine dose was 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ in 1 patient (0.4%), 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ in 44 (18%), 30 $\mu g \cdot kg^{-1} \cdot min^{-1}$ in 45 (18%), and 40 $\mu g \cdot kg^{-1} \cdot min^{-1}$ in 157 (64%). In 88 patients (36%), atropine was added. Patients who were using beta blocker therapy during the dobutamine stress test more frequently received atropine than did patients not receiving beta blocker therapy (54 of 105, 51%, vs 34 of 142, 24%, $P < .001$). A total of 181 patients (73%) achieved target heart rate. Achieving the target heart rate was not significantly different between patients with and without cardiac mortality (79 vs 72%, $P = .96$) and hard cardiac events (75 vs 80%, $P = .42$).

Side effects that occurred during dobutamine stress testing were generally self-limiting. These included

Table 1. Clinical characteristics

N = 247	Number (%)
Age (years)	71 ± 5
Male gender	129 (52)
Hypertension	102 (41)
Diabetes mellitus	47 (19)
Smoking	52 (21)
Hypercholesterolemia	74 (30)
Heart failure	40 (16)
LBBB	15 (6)
Beta blockers	105 (43)
Calcium channel blockers	111 (45)
ACE inhibitors	69 (28)
Diuretics	66 (27)
Nitroglycerine	101 (41)
Digoxine	23 (9)
History of myocardial infarction	89 (36)
History of coronary angioplasty	44 (18)
History of coronary artery bypass surgery	48 (19)

ACE angiotensin-converting-enzyme
LBBB left bundle branch block

atrial fibrillation in 5 patients (2%), short ventricular tachycardia (<10 complexes) in 6 patients (2.4%), and severe hypotension (decrease in systolic blood pressure >40 mm Hg) in 4 patients (1.6%). Minor side effects included nausea in 4 (1.6%), flushing in 3 (1.2%), and headache in 13 (5.3%). No patient experienced a myocardial infarction or ventricular fibrillation during or immediately after the stress test.

SPECT Results and Outcome

Abnormal MPI was detected in 140 patients (57%). A total of 20 (8%) patients showed reversible defects, 67 patients (27%) showed a fixed defect, while 53 patients (22%) showed both fixed and reversible defects. During a median follow up of 14 years (range 12-16), 168 (68%) patients died (all-cause mortality), of which 56 (23%) were due to cardiac causes. Nonfatal MI occurred in 19 (8%) patients. The Kaplan-Meier survival curves are shown in Figures 1, 2, and 3. The survival curves show that a normal MPI was associated with relatively low risk of all-cause mortality, cardiac mortality, and hard cardiac events. Conversely, elderly patients with an abnormal MPI had a significantly increased risk of all-cause mortality and cardiac events.

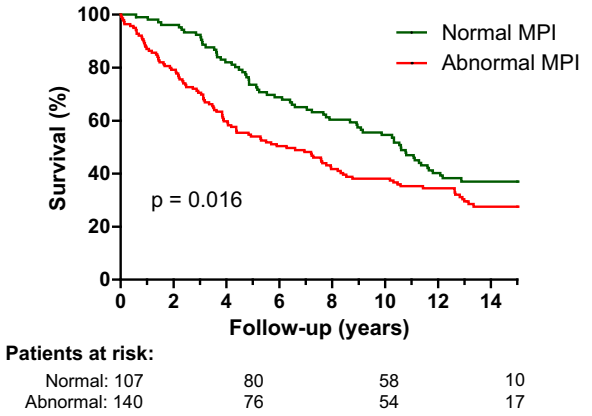

Figure 1. Kaplan-Meier survival curves for all-cause mortality.

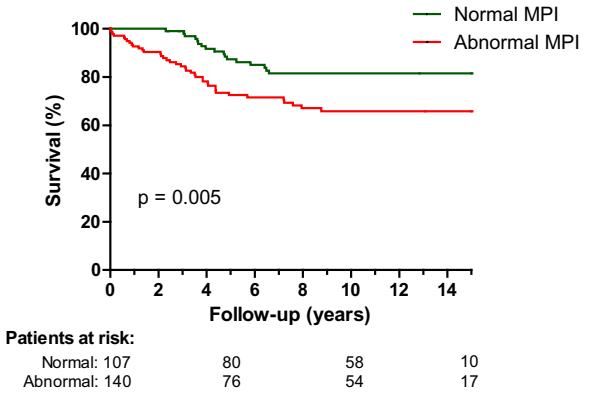

Figure 2. Kaplan-Meier survival curves for cardiac mortality.

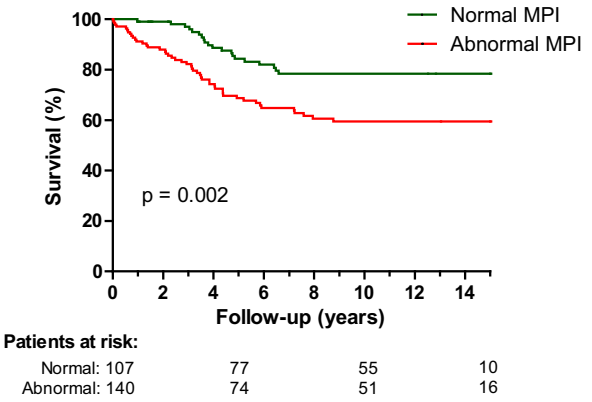

Figure 3. Kaplan-Meier survival curves for hard cardiac events (cardiac mortality and nonfatal myocardial infarction).

Predictors of Outcome

Univariable and multivariable predictors of all-cause mortality, cardiac mortality, and hard cardiac events are shown in Tables 2, 3, and 4, respectively.

Table 2. Univariable and multivariable predictors of all-cause mortality

Variable	Univariable	Multivariable			
		Clinical data	Model 1	Model 2	Model 3
Men	1.84 (1.30-2.61)	1.69 (1.19-2.38)	$P = .12$	$P = .07$	1.49 (1.02-2.19)
Prior MI	$P = .50$	$P = .43$	-	-	-
Diabetes mellitus	1.58 (1.05-2.38)	$P = .07$	-	-	-
Hypertension	1.88 (1.34-2.64)	1.76 (1.25-2.46)	1.83 (1.29-2.60)	1.77 (1.25-2.51)	1.72 (1.21-2.45)
Hypercholesterolemia	$P = .97$	$P = .66$	-	-	-
Smoking	1.49 (1.01-2.20)	$P = .06$	-	-	-
Heart failure	1.99 (1.32-3.01)	1.75 (1.16-2.65)	1.72 (1.13-2.61)	1.69 (1.10-2.57)	1.63 (1.06-2.51)
Stress test results					
Angina pectoris	$P = .46$	-	$P = .19$	$P = .28$	$P = .24$
ST-segment changes	$P = .41$	-	$P = .99$	$P = .80$	$P = .75$
Peak heart rate	$P = .37$	-	$P = .19$	$P = .60$	$P = .64$
Scan parameters					
Abnormal MPI	1.76 (1.24-2.51)	-	1.79 (1.22-2.64)	-	-
Fixed defect	$P = .14$	-	-	$P = .09$	-
Reversible defect	1.76 (1.24-2.51)	-	-	1.64 (1.13-2.38)	-
SSS*	1.20 (1.11-1.38)	-	-	-	$P = .11$

Statistically significant predictors of outcome are presented as hazard ratio (confidence interval), of all other variables the *P* value is presented.
- not included in the model, * per % myocardium increment, *MI* myocardial infarction, *MPI* myocardial perfusion imaging, *SSS* summed stress score

Table 3. Univariable and multivariable predictors of cardiac mortality

Variable	Univariable	Multivariable			
		Clinical data	Model 1	Model 2	Model 3
Men	$P = .16$	$P = .31$	-	-	-
Prior MI	$P = .51$	$P = .63$	-	-	-
Diabetes mellitus	2.17 (1.22-3.89)	$P = .07$	-	-	-
Hypertension	2.55 (1.19-4.37)	2.43 (1.42-4.17)	2.41 (1.40-4.17)	2.28 (1.32-3.92)	2.32 (1.34-4.01)
Hypercholesterolemia	$P = .47$	$P = .60$	-	-	-
Smoking	$P = .25$	$P = .09$	-	-	-
Heart failure	2.79 (1.56-4.99)	2.60 (1.45-4.65)	2.39 (1.32-4.30)	2.37 (1.31-4.27)	2.18 (1.19-4.00)
Stress test results					
Angina pectoris	$P = .93$	-	$P = .65$	$P = .88$	$P = .70$
ST-segment changes	$P = .50$	-	$P = .53$	$P = .76$	$P = .76$
Peak heart rate	$P = .87$	-	$P = .99$	$P = .90$	$P = .96$
Scan parameters					
Abnormal MPI	2.23 (1.26-3.94)	-	2.49 (1.39-4.48)	-	-
Fixed defect	$P = .34$	-	-	$P = .17$	-
Reversible defect	1.94 (1.14-3.33)	-	-	1.92 (1.11-3.33)	-
SSS*	1.11 (1.00-1.12)	-	-	-	1.09 (1.01-1.18)

Statistically significant predictors of outcome are presented as hazard ratio (confidence interval), of all other variables the *P* value is presented.
- not included in the model, * per % myocardium increment, *MI* myocardial infarction, *MPI* myocardial perfusion imaging, *SSS* summed stress score

Table 4. Univariable and multivariable predictors of hard cardiac events.

		Multivariable			
Variable	**Univariable**	**Clinical data**	**Model 1**	**Model 2**	**Model 3**
Men	1.70 (1.04-2.76)	$P = .07$	-	-	-
Prior MI	$P = .73$	$P = .83$	-	-	-
Diabetes mellitus	1.76 (1.01-3.05)	$P = .19$	-	-	-
Hypertension	2.31 (1.42-3.75)	2.24 (1.38-3.63)	2.16 (1.32-3.54)	2.02 (1.24-3.31)	2.00 (1.22-3.29)
Hypercholesterolemia	$P = .43$	$P = .59$	-	-	-
Smoking	$P = .28$	$P = .14$	-	-	-
Heart failure	2.24 (1.29-3.89)	2.11 (1.22-3.67)	1.90 (1.09-3.32)	1.90 (1.09-3.31)	$P = .05$
Stress test results					
Angina pectoris	$P = .77$	-	$P = .47$	$P = .65$	$P = .54$
ST-segment changes	$P = .48$	-	$P = .31$	$P = .91$	$P = .95$
Peak heart rate	$P = .41$	-	$P = .31$	$P = .44$	$P = .34$
Scan parameters					
Abnormal MPI	2.32 (1.38-3.91)	-	2.72 (1.59-4.66)	-	-
Fixed defect	$P = .13$	-	-	$P = .05$	-
Reversible defect	1.79 (1.10-2.93)	-	-	1.85 (1.12-3.04)	-
SSS*	1.11 (1.01-1.12)	-	-	-	1.09 (1.02-1.18)

Statistically significant predictors of outcome are presented as hazard ratios (confidence interval), of all other variables the *P* value is presented.
- not included in the model, * per % myocardium increment, *MI* myocardial infarction, *MPI* myocardial perfusion imaging, *SSS* summed stress score.

Among clinical variables, men, diabetes mellitus, hypertension, smoking, and heart failure were significant predictors of all-cause mortality (Table 2). Diabetes mellitus, hypertension, and heart failure were significant predictors of cardiac mortality (Table 3). Men, diabetes mellitus, hypertension, and heart failure were univariable predictors of hard cardiac events (Table 4). A multivariable model revealed that an abnormal MPI and reversible defect were powerful predictors of all-cause mortality (Table 2). A multivariable analysis also revealed that an abnormal MPI, reversible defect and SSS provided incremental prognostic information over that provided by clinical and stress test variables for predicting cardiac mortality (Table 3) and hard cardiac events (Table 4).

DISCUSSION

The main finding of this study is that dobutamine stress ^{99m}Tc-tetrofosmin SPECT provides long-term prognostic information for the prediction of all-cause mortality and cardiac events in elderly patients unable to perform exercise testing. Dobutamine stress MPI provided prognostic information incremental to clinical data and stress test results. Patients with a normal MPI had a relatively favorable long-term prognosis, in contrast to patients with an abnormal study who had a significantly increased risk of all-cause mortality and cardiac events. An abnormal MPI and the scan result reversible perfusion defect were strong significant predictors of all-cause mortality and cardiac events. Also the SSS was a strong long-term predictors of cardiac mortality and hard cardiac events.

In the aging population, CAD is a major health problem, and cardiovascular disease is still the leading cause of mortality in elderly patients.[17] As a result, elderly patients with known or suspected CAD are frequently encountered in a nuclear cardiology practice. Stress MPI is an important noninvasive technique for the evaluation of patients with known or suspected CAD. Elderly patients are frequently unable to perform an exercise test due to several comorbidities (e.g. obstructive lung disease, peripheral vascular disease). Dobutamine stress MPI is a feasible alternative for these patients and also for patients who have contraindications for vasodilator (dipyridamole or adenosine) stress testing.[3] The present study included 247 elderly patients unable to perform an exercise test. We found that dobutamine stress MPI had incremental long-term prognostic value additional to clinical variables and stress test results.

Several previous studies have evaluated the short or medium-term prognostic value of SPECT MPI in elderly

patients with a follow-up duration ranging from 4.4 to 6.4 years. Steingart et al.[5] studied 578 patients aged 65 years or older (mean age 70.7 ± 4.4 years) who underwent exercise MPI. A multivariable model revealed that age, male gender, limitation of exercise tolerance, and the number of ischemic segments on MPI were significant predictors of death or MI. The authors concluded that an abnormal MPI provided prognostic information during the 4-year follow-up period. Valeti et al.[6] followed 247 elderly patients with a mean age of 77 years undergoing exercise thallium-201 MPI. A total of 42 (17%) patients had a history of CAD (history of MI) compared to 89 (36%) patients in the current study. Also, patients without a previous percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) were included, while in the current study 37% had a previous coronary revascularization. In that study of Valeti et al.,[6] exercise MPI was accurate for risk stratification in elderly patients who were able to exercise during a median follow-up duration of 6.4 years.

A total of three studies have assessed the short- to medium-term cardiovascular outcomes after pharmacological stress MPI. De Winter et al.[7] studied cardiovascular outcomes in a total of 294 patients (median age 78 years) that underwent exercise ($n = 103$) or dipyridamole stress ($n = 191$) ^{99m}Tc-tetrofosmin SPECT. During a median follow-up of 25.9 months 47 deaths occurred of whom 27 cardiac deaths. The summed rest score (SRS) was a significant predictor of all-cause mortality and cardiac mortality. The authors concluded that gated SPECT provided independent and incremental information above clinical and perfusion SPECT. Nagao et al.[9] studied the outcomes of 175 patients (aged 75-85 years) that underwent exercise ($n = 49$) or vasodilator stress ($n = 126$) ^{99m}Tc-sestamibi SPECT. A total of 64 patients (37%) had a previous MI or coronary revascularization compared to 73% in the current study. During a mean follow-up of 3.4 years, SPECT results were predictive of cardiovascular outcomes. The results of those studies are in line with the current study, in that elderly patients with a normal SPECT have a relative good prognosis compared to patients with an abnormal SPECT who have an increased risk of all-cause mortality and cardiac events. In those studies, the maximum follow-up duration was limited to 6.4 years. Schinkel et al.[8] has described the 3.3 years cardiovascular outcomes of this cohort of 247 elderly patients. Dobutamine stress ^{99m}Tc-tetrofosmin SPECT provided incremental prognostic information for the prediction of total mortality and cardiac events. However, no data exist on the long-term prognostic value of pharmacologic stress MPI. The present study extends the observations drawn from these previous studies and demonstrates the long-term prognostic value of dobutamine stress MPI in elderly patients.

More recently, Kwon et al.[18] studied a Medicare cohort including 5,994 patients (age > 65 years) who underwent exercise ($n = 1,664$) or adenosine stress ($n = 4,280$) MPI. During a median follow-up of 2.4 years, the ability to exercise and the number of METs achieved were predictive of outcome. Among patients who were able to perform an exercise test, MPI did not provide incremental significant risk stratification. Several factors may explain why the findings in the study of Kwon et al. differ from the current findings. First, the current study included only patients who were unable to perform an exercise test, which is a marker of an adverse outcome in itself. Second, this study included a substantial number of patients with known CAD (36% had a previous myocardial infarction, 18% had previous coronary angioplasty, and 19% had previous coronary bypass surgery). Third, this study had a long-term and nearly complete follow-up which included information from the patient, the general practitioner, civil registries, and review of hospital records. The all-cause mortality rate during the long-term follow-up in the current study was 68% vs 6% during the median follow-up of 2.4 years in the previous study of Kwon et al. All these factors could have influenced the outcomes.

SPECT MPI is routinely used in conjunction with both ^{99m}Tc-sestamibi and ^{99m}Tc-tetrofosmin as tracers. The latter is used in the current study. Multiple studies have reported the prognostic value of ^{99m}Tc-sestamibi during dobutamine[19,20] or adenosine induced stress[21] in various patient subsets. In a previous study of our center, 473 patients were studied who underwent dobutamine stress ^{99m}Tc-sestamibi SPECT and were followed for a mean follow-up of 8[19] and 11 years.[20] A total of 44% of the patients had a previous MI and 35% had undergone previous revascularization. A total of 312 (66%) patients had abnormal MPI, defined as the presence of a fixed and/or reversible perfusion defect. The incremental prognostic value of dobutamine stress SPECT was maintained during a follow-up duration of 11 years. In the present long-term follow-up study, elderly patients with normal MPI had a maintained favorable event-free survival compared to patients with abnormal MPI. So, the present findings are consistent with these previous studies. Also, Hachamovitch et al.[21] studied 684 elderly patients (mean age 80.3 ± 4.1 years) who underwent ^{99m}Tc-sestamibi SPECT MPI. Of the 684 patients, 26% had a previous MI and 30% had prior revascularization. During a mean follow-up of 6 years, cardiac mortality rates were significant lower in patients with normal MPI in contrast to patients with abnormal MPI. The findings

of the current study extends the conclusions drawn from this study.

NEW KNOWLEDGE GAINED

Stress ^{99m}Tc-tetrofosmin MPI provides incremental prognostic information for the prediction of 14-year cardiovascular outcomes in elderly patients unable to perform exercise testing. Information on the presence, severity, and extent of perfusion abnormalities can be used for risk stratification of this high-risk patient group.

STUDY LIMITATIONS

The current study has limitations. First, all elderly patients were unable to perform exercise testing reflecting a high-risk population. The results of these study may not be applicable to other elderly patients. Second, no attenuation or scatter correction was used for MPI. Application of attenuation and scatter correction may have further improved the accuracy of SPECT MPI.[22] Third, due to the elderly patient population studied, the current results may not be extrapolated to younger patients. Fourth, gated SPECT was not routinely used in our laboratory at the time that this study was performed. Previous data have demonstrated the superiority of gated SPECT to non-gated SPECT in outcome prediction. However, in the current study, we analyzed the prognostic value of non-gated SPECT. Finally, the examined patient population was relatively small. This could have influenced the outcome of the multivariable analysis.

CONCLUSIONS

Dobutamine stress MPI provides incremental prognostic information for the prediction of all-cause mortality and cardiac events on the long-term outcome in elderly patients unable to perform exercise testing. Patients with a normal MPI have a favorable prognosis of long-term outcome, in contrast to patients with an abnormal study.

Disclosure

All authors declare no conflicts of interests.

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